REMARKS/ARGUMENTS

The Office Action of May 7, 2003 has been received and considered. In the Office Action, claims 1-16 were rejected under 35 U.S.C. §112 and either 35 U.S.C. §102(b) or 35 U.S.C. §103(a).

Claims 1, 5, 9, 10, 13 and 14 have been amended. Claims 1-16 remain pending. Reconsideration of the application is respectfully requested.

Rejections under 35 U.S.C. §112, first paragraph

Claims 5-8 have been rejected under 35 U.S.C. 112, first paragraph, as including subject matter that was not described in the specification in such a way as to reasonably convey to one of ordinary skill in the art that the inventors, at the time the application was filed, had possession of the invention as claimed. Specifically, it is asserted in the Office Action that the phrase "cancer cell specific identifying agent" does not find support in the originally filed specification. However, when the specification is read by one of ordinary skill in the art, it is clear that the applicants had possession of the invention as claimed in claims 5-8 at the time the application was filed.

Applicants note that the specification need not provide *ipsis verbis* support for the language set forth in the pending claims. Instead, the claims need only be supported by the originally filed specification when the specification is read by one of ordinary skill in the art. Support for the phrase in question can be found in two different portions of the specification. First, on page 10, lines 23-34, the specification expressly recites that the present invention includes:

> a method of identifying atypical or cancerous cells . . . using an identifying agent, for example, monoclonal antibodies or other molecules directed against overexpressed or stage-specific cellular epitopes or targets such as . . . tumor specific antigens and the like. (Page 10, lines 23-27)

This portion of the specification, when read in context with the other portions of the specification, clearly sets forth that the applicants had the concept of using a cancer specific identifying agent at the time of filing the present application.

In a second portion of the specification, page 11, lines 13 and 14, for example, the specification indicates that the identifying agent can bind specifically to a cancer specific targeting agent that has bound to a cancer or precancerous cell. Therefore, the specification identifies that the inventors contemplated using identifying agents that would bind to only cancerous or precancerous cells. Thus, because the identifying agents bind to targeting agents that are specifically bound to cancerous or precancerous cells, it would be understood by one of ordinary skill in the art that the applicants had possession of cancer specific identifying agents at the time the present invention was filed.

For all of the above-discussed reasons, when the above-discussed portions of the specification are read in light of page 14, lines 19-34 and page 15, lines 1-23, withdrawal of the outstanding rejection is requested.

Claims 1-8 were rejected under 35 U.S.C. §112, first paragraph, as including subject matter that was not described in the specification in such a way as to reasonably convey to one of ordinary skill in the art that the inventors, at the time the application was filed, had possession of the invention as claimed. Specifically, the Office Action suggests that the claims are not supported by the specification because these claims recite "pre-malignant or malignant cells"

within a breast duct or breast ductal network instead of "pre-malignant or malignant breast cancer cells." It is unclear to the undersigned how a breast duct or breast ductal network can include pre-malignant or malignant cells that are not considered pre-malignant or malignant breast cancer cells. Therefore, no amendments to claims 1-8 appear necessary. Nevertheless, in order to expedite prosecution of the application, applicants have made editorial amendments to claims 1 and 5 to include the phrase "breast cancer" even though such amendments are not necessary. Withdrawal of the rejection is requested.

Claims 1-16 were rejected under 35 U.S.C. §112, first paragraph, as including subject matter that was not described in the specification in such a way as to reasonably convey to one of ordinary skill in the art that the inventors, at the time the application was filed, had possession of the invention as claimed. Specifically, the Office Action suggests that the specification does not provide support for the concept of the unbound portion of the agent or compound being eliminated or exited from within a breast duct or breast ductal network. Claims 1, 5, 9 and 13 have been amended to recite that the detecting and determining steps occur after the unbound delivered agent or compound are no longer present within the breast duct or breast ductal network. The specification, including the examples, provides support for claims 1-16. Therefore, the original specification indicates that the applicants had the invention as claimed in their possession at the time the present application was filed. Withdrawal of the rejection is requested.

Rejections under 35 U.S.C. §112, second paragraph

Claims 10 and 14 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for lacking antecedent basis for the phrase "therein detecting." Claims 10 and 14 have been amended to provide antecedent basis for the language recited in claims 10 and 14. Withdrawal of the rejection is requested.

Claims 1-16 have also been rejected under 35 U.S.C. §112, second paragraph, for not including, what are asserted to be, one or more essential steps. These steps are listed in the Office Action. As previously discussed, "essential matter" is not merely those elements or steps that form a portion of the invention or that are discussed in the specification. Instead, "essential matter" is defined in M.P.E.P. §2172.01 as elements, steps or the like that are described by the applicant(s) in the specification as essential to practicing the invention. Therefore, in order for a step in the method to be considered essential matter, the applicant(s) must have disclosed in the specification or arguments that the step in question was "essential" to practicing the invention. The statements of the applicant(s) are the test of whether not something is essential, not the opinion of the Examiner that is not based on an express statement of the applicant(s).

Applicants have amended claims 1 and 5 to include certain steps for clarity of the pending claims. Applicants do not submit that the steps added to these claims are essential. Instead, these steps have been recited to improve the clarity of the pending claims. Specifically, claims 1 and 5 have been amended to recite steps in which the bound compound or agent has been detected after the unbound compound or agent is no longer present within the breast duct or breast ductal network. It is submitted that the relationships between the introduction and binding

of the agent or compound to the premalignant cells or the malignant cells and the detecting of this binding after any unbound agent or composition is no longer present in the breast duct or breast ductal network is clearly recited in claims 1-8. No amendment was needed to claims 9 and 13 in view of the already recited "determining" step.

In the Office Action, it was asserted that claims 1-16 should be amended to include a step of correlating the data obtained in the detecting step to the anatomy of the patient because this step is "essential" to the method. In support of this position, the Office Action identifies that this step is discussed in both of the exemplary methods set forth in the specification. However, such an amendment is not necessary.

First, the presently pending claims recite a step of either (1) identifying the location of the premalignant or malignant cells or (2) identifying the location of lymph node involvement. One of ordinary skill in the art would clearly understand how to perform the methods recited in the pending claims, including the "identifying the location" steps, such that the position of the detected cells or the involved lymph nodes within the patient are identified when these claims are read in light of the specification. Second, the specification does not recite that a correlation step in addition to the locating step is essential to the invention. Page 8, lines 6-9, of the specification clearly recites that the location of the premalignant cells, the malignant cells and the involved lymph nodes can be identified by performing a MRI, PET or other known means. Additional support for alternative identification techniques is found on page 11. Therefore, contrary to the position taken in the Office Action, the steps set forth in the two examples contained within the specification are merely examples of how the location of the premalignant and malignant cells

can be determined and are not essential elements of the claimed methods as "essential" is defined in the MPEP.

It appears that the Examiner has taken the position that because a step is set forth as part of an example in the specification of the pending application, the step of the exemplary method is *per se* essential. Authority for such a position must be provided. Applicants request that authority for the position that every element of a disclosed example within a specification rises to the level of an essential element as a result of its inclusion in an exemplary method despite the fact that the Applicants have not disclosed in the specification or other statements that all of the steps in the exemplary methods are essential. However, Applicants submit that no such authority exists, and that the elements required in the Office Action are not essential.

In view of the clear teachings set forth in the specification regarding the techniques that can be used to identify the location of bound compounds or agents, all of the steps set forth in the exemplary methods cannot fairly be considered "essential matter" under MPEP §2172.01. Hence, amendments to the pending claims to include the asserted "correlating" step are not required to clearly and completely recite the methods according to the present invention in view of the instant specification and the prior art. For all of the above-discussed reasons, withdrawal of the rejections under 35 U.S.C. §112, second paragraph, is requested.

Again, as previously discussed, the burden of making a showing that the elements in question are not essential has not shifted to the applicants because a prima facie case has not been established. The mere assertion that the steps in an example provided in the specification are essential, absent some legal support for this position or a statement set forth in the specification, does not rise to the level of a prima facie case. Therefore, no such prima facie case

has been established. For all of the above-discussed reasons, withdrawal of the rejections under 35 U.S.C. §112, second paragraph, is requested.

Claims 9-16 have also been rejected under 35 U.S.C. §112, second paragraph, as failing to set forth the subject matter that applicants regard as their invention. These claims have been rejected, as best can be understood, because they do not correspond to a statement set forth in Paper No. 16, filed December 4, 2001, that was clearly misinterpreted by the Examiner. When the statement in question is read in context and in light of the specification, it is clear that the undersigned was distinguishing the methods of the present invention that include identifying only the location of (1) premalignant or malignant cells (claims 1-8) or (2) the involved lymph nodes of patients diagnosed with premalignant or malignant cells (claims 9-16) from those methods that stain the entire breast duct and the lymph nodes to identify these portions of the body for surgical removal. Applicants were clearly stating that the methods according to the present invention do not identify the portions of the breast duct that are free of premalignant or malignant cells or the remainder of the lymph nodes that are not involved but that would otherwise be identified by conventional nodal mapping. Additionally, applicants' remarks are consistent with the specification and the pending claims. Withdrawal of the rejection is requested.

Rejection under 35 U.S.C. §102

Claims 5-8 were rejected under 35 U.S.C. §102(b) as being clearly anticipated Hou et al. as evidenced by VanZee et al. and Canto, et al. Hou discloses a method of performing

galactography before excision of a duct in patients with nipple discharge. During the galactography method discussed in Hou, a discharging breast duct is identified and a contrast material is introduced into this duct. Then, a mammogram is performed on the patient. When the mammogram identifies premalignant and/or malignant cells within a breast duct, the breast duct is prepared for removal. In order to assist the surgeon in finding the boundary of the breast duct that needs removal, methylene blue is introduced into the breast duct via a catheter. The function of the methylene blue is to stain the breast duct and identify the boundary of the breast duct so that the surgeon can remove the breast duct from the patient. The methylene blue is not used to identify the location of the premalignant or malignant cells within the breast duct.

Also, in the method of Hou, the introduced methylene blue is intended to remain completely within the duct that is to be removed so that it shows the boundary of the duct, while not staining portions of the patient's anatomy that do not require removal. Therefore, Hou does not teach that the methylene blue is allowed to bind to some portions of the duct and that the unbound methylene blue is allowed to be eliminated from the duct. If the methylene blue were allowed to pass into other parts of the body as suggested in the Office Action, the portions of the body that received the eliminated methylene blue would be erroneously marked for removal from the body of the patient. This erroneous marking would be a critical surgical error. Therefore, one of ordinary skill in the art would not understand the method of Hou to include a step of allowing the methylene blue stain to be eliminated into parts of the body that are not intended to be removed as suggested in the Office Action.

Additionally, the Hou method does not teach the step of detecting the presence of the identifying agent bound to premalignant or malignant cells within said at least one duct or ductal

network **after** said unbound portions of the delivered identifying agent are no longer present within said at least one breast duct. Instead, Hou discloses the step (mammogram) used to detect the presence of the premalignant or malignant cells occurs before the methylene blue is introduced into the breast duct. Therefore, it only follows that the methylene blue is not used in the Hou method to identify the location of the premalignant or malignant cells since the mammogram is used during the Hou method to identify the location of these cells – the methylene blue is only used to identify the boundary of the duct that needs removal. As a result, the method of Hou does not anticipate claims 5-8.

Moreover, contrary to the position taken in the Office Action, methylene blue is not cancer cell specific within a breast duct. In the Office Action, it is submitted that the phrase "cancer cell specific identifying agent" is not defined in the specification. As a result, the position was taken that anything which stains a duct and shows the topography of a duct is a "cancer cell specific identifying agent."

Applicants submit that one of ordinary skill in the art clearly understands the phrase "cancer cell specific identifying agent that is cancer cell specific within a breast duct or breast ductal network" to mean an agent that binds only to cancerous cells and not healthy cells within a breast duct or breast ductal network. The level of skill cannot be lowered to that of a conventional dictionary as done in the Office Action in order to shoehorn Hou into a rejection. As clearly understood by one of ordinary skill in the art, methylene blue is a not specific to cancer cells - it does not bind only to cancer cells within a breast duct or breast ductal network. Therefore, methylene blue is not a cancer cell specific identifying agent as recited in amended claim 5. Hence, the step of introducing the methylene blue into the duct does not anticipate the

step of "providing a premalignant or malignant cancer cell specific identifying agent" as recited in claim 5.

Additionally, a publication to Canto et al. was cited to support the position taken in the Office Action. However, the publication to Canto is specific to the esophagus. Canto discloses that the esophagus is not normally stained by methylene blue. However, cancerous cells lining the esophagus can be stained by methylene blue. Therefore, it was asserted in the Office Action that methylene blue is cancer specific because it stains cancerous cells within the esophagus while not staining healthy esophageal cells. But, the present invention relates to the introduction and performance of cancer specific agents/compounds within a breast duct or breast ductal network. Methylene blue stains healthy ductal epithelial cells, for example, and malignant ductal epithelial cancer cells the same within the breast duct. Methylene blue is not cancer specific within a breast duct. Clearly, the teachings of Canto are not applicable to the present invention. Similarly, it is clear that the esophageal specific disclosure of Canto has been improperly stretched to suggest that methylene blue is cancer specific in all areas of the body.

Claims 5-8 are clear, supported by the originally filed specification, find written description in the originally filed specification and are not anticipated by Hou. For all of the above-discussed reasons, withdrawal of the rejection is requested.

Rejections under 35 U.S.C. §103

Claims 1-16 were rejected under 35 U.S.C. §103(a) as being unpatentable over Hou in view of Allan et al. and Vitetta et al. as evidenced by Krag et al. As discussed above, Hou

discloses a method of performing galactography on a patient. In the Hou method, the contrast material is introduced into the duct before the mammogram is performed. If the mammogram identifies that a surgical excision of a duct is necessary, methylene blue is introduced into the breast duct in question. After the introduction of the methylene blue, a precise surgical excision of the dye-stained ducts and lobules is performed. The methylene blue only maps the duct to be removed by the invasive surgical procedure. The methylene blue is not a targeting molecule coupled to an identifying agent that identifies the cancerous cells. Similarly, the methylene blue is not a cancer cell specific identifying agent.

Allan discloses a method of radioimmunolocalization of a breast duct to facilitate surgical excision of tissue including and surrounding malignant breast cancer cells. The Office Action suggests that it would have been obvious to modify the method of Hou with the step of introducing the agent of Allan into the breast duct through a ductal opening. However, as discussed below, a prima facie case of obviousness has not been set forth because (1) no motivation exists for the asserted combination, (2) impermissible hindsight has been used to pick and choose portions of the Allan method while ignoring others, (3) no expectation of success exists for this modification and (4) the steps needed to prepare the agent disclosed in Allan's method contradict the method set forth in Hou.

It appears that Hou is being relied upon to teach the concept of intraductal introduction of a material. Allan discloses a method for developing an antibody that is systemically introduced into the body. In order to perform the method disclosed in Allan, the patient is first subjected to a mammogram. Then, if the mammogram identifies questionable cells, fine needle aspiration (FNA) or a core biopsy is performed on the tumor in the breast. As is well known in the art,

FNA is a very uncomfortable procedure for the patient and can lead to the spreading of cancerous cells within the body. After the FNA or biopsy has been performed in the Allan method, the collected samples are analyzed. An antibody based on the fine needle aspirate is then developed. The developed antibody is then systemically introduced into the body.

FNA **is not** a procedure that is performed within a breast duct because FNA would cause (1) the duct to be punctured, (2) the duct to collapse and (3) severe injury to the patient. Therefore, the steps needed to prepare the antibody of Allan could not be performed on the cancerous ductal cells discussed in Hou.

As can be seen from the above discussions and a fair read of the cited publications, the prior art does not provide motivation for the asserted combination. The only motivation for the asserted combination is that disclosed in the specification of the instant application. For example, the motivation set forth in the outstanding Office Action is almost verbatim what applicants have disclosed as the benefits of the present invention. Allan and the systemic introduction of its antibody does not teach any of the benefits or the motivation discussed in the Office Action. Additionally, these benefits were not known to one of ordinary skill in the art because no one had introduced the recited agent or compound through a ductal opening prior to the invention of the applicants. Therefore, the general state of the prior art could not have provided the asserted motivation. Since no motivation exists in the prior art and the only suggestion is that provided by the applicants, the rejection is necessarily based on impermissible hindsight and the rejection must be withdrawn. See In re Vaeck, 974 F.2d 488 (Fed. Cir. 1991).

The Office Action suggests that motivation can be found in the increased specificity provided by the antibody developed using the Allan method. However, (1) the antibody of Allan

cannot be prepared as disclosed because the cancerous cells are within a breast duct; and (2) Allan only teaches introducing the developed antibody systemically and obtaining the specificity through systemic introduction. Allan's step of systemically introducing the antibody cannot be ignored. Allan has to be taken as a whole. Without some teaching in the prior art for introducing the antibody through a breast duct opening, no motivation exists for introducing the antibody into the patient anyway but systemically. Therefore, at best, one of ordinary skill in the art may have been motivated to modify the method of Hou to include a step of systemically introducing the antibody of Allan, but not introducing intraductally as recited.1 Again, Allan's teaching of systemically introducing the agent cannot be ignored and cast aside as has been done in the formulation of the outstanding rejection because the prior art does not provide any expectation of success for the intraductal introduction of the antibody instead of the systemic introduction. Absent some teaching in the prior art and expectation of success, the rejection cannot be sustained. See In re Vaeck, 974 F.2d 488 (Fed. Cir. 1991). The position has been taken in the Office Action that "there does not appear to be a reason one of ordinary skill in the art would not have had a reasonable expectation of success" is not the test. It is the PTO's burden to affirmatively provide an expectation of success. Since no such affirmative expectation has been provided, the asserted prima facie case of obviousness has not been established.

Additionally, the Office Action suggests that one of ordinary skill would modify the methylene blue of Hou with the antibody of Allan because the use of the antibody would increase the specificity of the location of the identified cancerous cells. However, the method of

1 As discussed below, the applied references are not combinable even to arrive at the systemic introduction of Allan's antibody.

Hou does not require additional specificity. The method of Hou only needs to identify that cancerous cells are present in the duct in question. Then, once cancerous cells are identified in a duct, the methylene blue is introduced into that duct to indicate the boundary of the duct so that the duct can be surgically removed with a level of precision. The method of Hou only needs to identify the presence of cancerous cells, it does not require the identification of the specific location of the cancerous cells. Therefore, the asserted need for increased specificity of the location of the cancerous cells within the duct does not exist. As a result, no motivation exists for the suggested combination because one of ordinary skill in the art would not need to increase the specificity of the location of the cancerous cells in the Hou method because the method of Hou only needs to identify the presence of cancerous cells within a duct so that the entire duct can be removed. Additionally, replacing the methylene blue with an antibody that only binds to cancerous cells and does not stain the entire duct in the method of Hou would destroy the method of Hou because the surgeon would not be able to identify the boundary of the duct and safely remove the duct. Similarly, one of ordinary skill in the art would not have been motivated to remove anything less than the entire duct in the method of Hou because doing so would cause the duct to be punctured, the duct to collapse and the health of the patient jeopardized.

The rejection is also not sustainable for the following reasons. The method of Hou requires the mammogram to be performed after the identifying agent - contrast material - has been introduced into the breast duct. To the contrary, the steps of the Allan method require that the mammogram be performed before the agent, to be used in the Hou mammogram, is developed so that the tumor accessed during the FNA step can be located. The modification suggested in the Office Action would require that the steps of the Hou method be modified so

that the mammogram of Hou is performed before the agent used in the Hou mammogram is prepared and introduced into the body. The mammogram of Hou cannot be performed without its identifying agent - its contrast material. Additionally, no need exists for performing multiple mammograms. The asserted modification contradicts the teachings of Hou and would render its method inoperable. Additionally, one of ordinary skill in the art would not have been motivated to perform FNA on a region within a breast duct because such action would cause the duct to collapse and the patient to be injured. Therefore, such a modification would not have been obvious to one of ordinary skill in the art.

Like the disclosures of Hou and Allan, the disclosure of Vitetta et al. (Vitetta) does not teach introducing a targeting molecule coupled to an identifying agent or a cancer specific identifying agent into a breast through a breast duct. Therefore, like Allan, Vitetta would not have motivated one of ordinary skill to modify the method of Hou to arrive at the methods recited in claims 1-16. For all of the above-discussed reasons, withdrawal of the rejection is requested.

Claims 1-16 are rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,168,779 to Barsky et al. (Barsky) in view of Allan and Lasfargues et al. as evidenced by Krag et al.

Barsky is directed to and discloses a method of identifying ductal orifices on a nipple surface. While Barsky does include a statement that diagnostic, therapeutic or other materials could be instilled into the duct, Barsky does not disclose or contemplate a method of identifying the location of premalignant or malignant breast cancer cells within a breast duct or ductal network as recited in claims 1-16. Hence it cannot disclose such a method that includes the step

of delivering either a targeting molecule coupled to an identifying agent or a cancer specific identifying agent into a breast through a breast duct.

The disclosures relied upon in the Office Action on columns 3 and 4 of the Barsky patent relate to the location and identification of ductal openings. The cited markers are specific to ductal epithelial cells, not premalignant or malignant cells. These disclosures do not and cannot be fairly considered to disclose steps for determining if the epithelial lining of the duct includes premalignant or malignant cells. These disclosures only disclose ductal opening identification. The very broad interpretation of these statements set forth in the Office Action cannot be sustained when the patent is taken as a whole. For example, the disclosure of the patent to Barsky has been erroneously extended to suggest that the identification of ductal openings by locating areas of ductal epithelial cells also discloses the step of identifying premalignant and malignant ductal epithelial cells. Clearly, the patent to Barsky does not include such a disclosure.

As discussed above, Allan discloses a method for systemically introducing an antibody into a patient for locating cancerous cells within the body. Allan does not disclose that the antibody can be introduced into the patient other than systemically. Neither reference provides any teaching of providing the recited cancer specific targeting molecule and identifying agent or cancer specific agent into the breast by intraductal introduction. Therefore, Allan would not have motivated one of ordinary skill in the art to modify the method of detecting ductal orifices on the nipple surface with a method of systemically introducing an antibody into a patient to detect the presence of cancerous cells.

The disclosure of the publication to Lasfargues is relied upon to teach that ductal breast cancer can originate in the epithelial cells of the breast. However, this teaching does not provide any motivation for the suggested combination.

No teaching exists in either Barsky, Allan or Lasfargues that would have lead one of ordinary skill to modify the method of Barsky to arrive at the method recited in claims 1-16. This outstanding rejection is clearly based on impermissible hindsight. As can be seen, the applicants' disclosure has been improperly used as a road map through the prior art during the formulation of the present rejection. It is well settled that the prior art, not applicants' disclosure, must provide the teaching and motivation for the asserted combination. See In re Vaeck, 947 F.2d 488. Additionally, there is no expectation of success for the asserted combination. Withdrawal of the rejection is requested.

Claims 1-16 were rejected under 35 U.S.C. §103(a) as being unpatentable over Hou in view of McQuarrie et al. and Krag et al. As discussed above, the publication to Hou only discloses the introduction of a contrasting agent and methylene blue through a duct during a specific procedure - galactography. Therefore, Hou does not disclose all that it is relied upon to teach and the rejection should be withdrawn.

Like Allan, McQuarrie discloses the use of an antibody that is systemically introduced into a patient to determine the location of cancerous cells in response to an application of radiation. However, like Allan, McQuarrie does not disclose or contemplate the introduction of the antibody into a breast through a breast duct.

No motivation exists for modifying the method of Hou with the antibody disclosed in McQuarrie. The intravenous introduction of the antibody of McQuarrie cannot be ignored. Like

Allan, McQuarrie must be taken as a whole. McQuarrie teaches that the developed antibody is introduced systemically into the body. Without some teaching in the prior art for introducing the antibody through a breast duct opening, no motivation exists for introducing the antibody into the patient anyway but systemically. The most that the prior art can teach one of ordinary skill in the art is to introduce the antibody systemically or to introduce a stain used to mark the parameters of a duct for surgical removal of the duct through a ductal opening. But, the prior art does not teach the step of introducing a coupled compound including a targeting molecule and an identifying agent into a breast through a ductal opening. Therefore, the rejection cannot be sustained.

Additionally, the asserted combination would fail to teach the steps of the recited methods. As discussed, the method of Hou introduces the contrast material into the duct and allows it to remain in the duct until after the presence of any cancerous cells has been identified. McQuarrie does not teach removing or allowing unbound portions of the introduced antibody to exit the breast duct before the presence and location of the cancerous cells are identified. Therefore the asserted combination would not have been obvious to one of ordinary skill in the art would not have arrived at the recited method. For example, the asserted combination fails to teach the steps of (1) detecting the presence of the compound or identifying agent bound to premalignant or malignant cells within said at least one duct or ductal network after the unbound portions of the delivered compound are no longer present within said at least one breast duct; and (2) identifying the location of the bound premalignant or malignant cells or the lymph node involvement.

As discussed above with respect to Allan, only applicants' own specification provides the motivation and an expectation of success that is relied upon in the Office Action. The prior art does not provide the required teaching and motivation. The prior art does not include a suggestion that would have motivated one of ordinary skill in the art to modify a reference that teaches galactography in order to arrive at the claimed method. Such a modification would destroy the galactography procedure disclosed in Hou - the purpose of Hou. Therefore, the outstanding rejection can only be based on impermissible hindsight and the rejection must be withdrawn.

Claims 1-16 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5, 31 and 32 of co-pending U.S. Patent Application No. 09/565,642 in view of Slavin-Chiorini, Allan and Krag. A terminal disclaimer may be filed at the time that claims in either or both applications are indicated to be allowable.

For all of the above-discussed reasons, applicants respectfully submit that claims 1-16 are allowable and that the application is now in condition for allowance. A notice to this effect is earnestly solicited.

If any questions or issues remain, the resolution of which the Examiner feels would be advanced by a conference with Applicants' attorney, the Examiner is invited to contact Applicants' attorney at the number noted below.

It is believed that no fee is required for this submission. If any fees are required or if an overpayment is made, the Commissioner is authorized to debit or credit our Deposit Account No. 19-0733, accordingly.

Respectfully submitted,

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